O,O-Diethyl dithiophosphate

CAS # 298-06-6

Test plan

Bayer CropScience LP

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Executive Summary

Bayer CropScience LP (Bayer) hereby submits for review and public comment their test plan for O,O-diethyl dithiophosphate (CAS# 298-06-6) under the Environmental Protection Agency's High Production Volume (HPV) Chemical Challenge Program.

IUPAC Name	Common Name	Abbreviation	CAS#
O,O-diethyl dithiophosphate	diethyl acid	DEA	298-06-6

O,O-diethyl dithiophosphate is used as an intermediate in the production of an agricultural insecticide.

In consideration of animal welfare concerns to minimize the use of animals in the testing of chemicals, Bayer has conducted a thorough literature search for all available data, published and unpublished. Bayer has also performed an analysis of the adequacy of the existing data. Existing data indicates that this chemical is of high concern for aquatic toxicity, low concern as Persistent Organic Pollutants (POP), moderate concern for skin irritation, and low concern for acute mammalian toxicity. In a separate submission, Bayer has explained in detail that this substance is a closed-system intermediate and therefore a reduced data set is required. To fulfill the SIDS data set, an "*in vitro* Mammalian Cytogenetic Test" (OECD 473) and Teratogenicity study (OECD 414) on DEA is proposed for purposes of the HPV Program.

Closed System Intermediate Chemical Status

A separate document is being submitted to EPA to describe the process, sites, and transport of DEA to explain "closed-system" intermediate status. This information is considered Confidential and therefore is not available to the public in this document.

Data Review

Physicochemical properties:

The properties of DEA can be found in various online databases and some endpoints were calculated with EPIWin Modeling Program. DEA is a liquid at ambient temperatures and decomposes before boiling. The calculated octanol/water partition coefficient is 1.17 and only the salt form is soluble in water. Data is available for all endpoints, no additional testing is proposed for purposes of the HPV Program (See Table 1 and IUCLID document).

Environmental Fate:

Photodegradation was calculated as a half-life of 1.4 hours for DEA. Fugacity modeling demonstrates partitioning to the soil and water compartments. Biodegradation modeling demonstrates that DEA is biodegradable. In addition, a well documented study on various thiophosphates indicated complete mineralization within three weeks by acclimation. A water stability study demonstrated the nature of hydrolysis involves the attack of water molecule on the phosphorus of the di-ester involving P-O bond fission. Data is available for all endpoints, no additional testing is proposed for purposes of the HPV Program (See Table 1 and IUCLID document).

Ecotoxicology:

Aquatic studies have been performed on *Salmo gairdineri, Poecilia reticulata* and on *Daphnia magna*. The 24 hour LC50 of *Daphnia magna* = 0.54 mg/l (highly toxic). There are no studies on algae, however since DEA is highly toxic to *Daphnia*, additional testing on algae will not provide useful or relevant data for risk assessment. No additional testing is proposed for purposes of the HPV Program (See Table 1 and IUCLID document).

Mammalian Toxicology:

Toxicity studies in animals show that DEA is of low acute toxicity by all routes of exposure: oral LD_{50} 4510 mg/kg (rat); inhalation LC_{50} 1640 mg/m^3 (rat); and dermal LD_{50} > 2000 mg/kg (rabbit). (See Table 1 and IUCLID document).

There is an Ames study on DEA to fill the mutagenicity endpoint. No studies on chromosome aberration were located. An "*in vitro* Mammalian Cytogenetic Test" (OECD 473) on DEA is proposed for purposes of the HPV Program (See Table 1 and IUCLID document).

There were no repeat dose, fertility, nor developmental studies found. Since DEA is a closed system intermediate, the repeat dose and fertility studies are waived. A "Teratogenicity" study (OECD 414) on DEA is proposed for purposes of the HPV Program. (See Table 1 and IUCLID document).

"Beyond SIDS" Endpoints:

Studies have been performed to investigate skin and eye irritation on DEA and found to be irritating to the skin and eyes of rabbits. (See Table 2 and IUCLID document).

Exposure:

Since DEA is a closed-system intermediate, potential for exposure is minimal. Occupational exposure is controlled by good industrial hygiene practices and engineering controls. Environmental releases are controlled/prevented by engineering controls and careful monitoring. DEA is not present in the finished product, therefore there are no potential downstream exposures. DEA is not expected to pose a risk to human health or the environment during manufacture, formulation, and under normal conditions of anticipated use, if the recommended safe use and handling procedures are followed.

Conclusion

Existing data indicates that this chemical is of high concern for aquatic toxicity, low concern as Persistent Organic Pollutants (POP), moderate concern for skin irritation, and low concern for acute mammalian toxicity. In a separate submission, Bayer has explained in detail that DEA is a closed-system intermediate and therefore a reduced data set is required. To fulfill the SIDS data set, an "*in vitro* Mammalian Cytogenetic Test" (OECD 473) and Teratogenicity study (OECD 414) on DEA is proposed for purposes of the HPV Program.

Table 1. Available data for DEA

Endpoint	DEA (CAS# 298-06-6)
Physical-Chemical Data	
Molecular weight	186.23
Physical state	liquid
Melting Point	Not applicable
Boiling Point	105-108 ºC @ 20 hPa
Vapour Pressure	.077 hPa @ 25 ºC
Partition Coefficient ($logP_{ow}$)	1.17
Water Solubility	insoluble
Environmental Fate	
Photodegradation	T ½ = 1.4 hours
Fugacity (distribution)	Air – 1.06 % Water – 39.5% Soil – 59.3% Sediment – 0.152%
Biodegradability	Inherently biodegradable
Water Stability	See IUCLID document
Ecotoxicology	
Acute Fish Toxicity 96 hrs LC_{50}	*Salmo gairdineri* 310-330 mg/l *Poecilia reticulata* 79 mg/l (24 hours)
Acute Invertebrate Toxicity 24 hrs LC_{50}	*Daphnia magna* 0.54 mg/l
Algal Toxicity 96 hrs LC_{50}	No data
Mammalian Toxicology	
Acute Toxicity	Oral LD_{50} = 4510 mg/kg (rat) Inhalation LC_{50} = 1640 mg/m3 (rat) Dermal LD_{50} >2000 mg/kg (rabbit)
Mutagenicity	Ames (± activation) = negative
Chromosome Aberration	No data
Repeated Dose Toxicity	No data
Reproductive Toxicity	No data
Developmental Toxicity	No data

* Robust summaries and References can be found in the IUCLID document.

Table 2. "Beyond SIDS" data for DEA

Endpoint	DEA (CAS# 298-06-6)
Skin Irritation	Slightly irritating (24 hrs, rabbit)
Eye Irritation	Highly irritating (24 hrs, rabbit)

* Robust summaries and References can be found in the IUCLID document.

Table 3. Test Plan for DEA

Endpoint	Data Availability	Acceptable	Planned testing
Physical-Chemical Data			
Melting Point	✓	✓	
Boiling Point	✓	✓	
Vapour Pressure	✓	✓	
Partition Coefficient ($logP_{ow}$)	✓	✓	
Water Solubility	✓	✓	
Environmental Fate			
Photodegradation	✓	✓	
Fugacity	✓	✓	
Biodegradability	✓	✓	
Water Stability	✓	✓	
Ecotoxicology			
Acute Fish Toxicity	✓	✓	
Acute Invertebrate Toxicity	✓	✓	
Algal Toxicity			Derogation statement
Mammalian Toxicology			
Acute Toxicity	✓	✓	
Mutagenicity	✓	✓	
Chromosome Aberration			OECD 473
Repeated Dose Toxicity	Not required 'Closed system intermediate'		
Reproductive Toxicity	Not required 'Closed system intermediate'		
Developmental Toxicity			OECD 414

✓ = data available and considered adequate.